MEMORY SYSTEMS

"....memory is, per se, a biological fact - by accident, a psychological fact....The disorders and maladies of this faculty, when classified and properly interpreted, are no longer to be regarded as a collection of amusing anecdotes of only passing interest. They will be found to be regulated by certain laws which constitute the very basis of memory, and from which its mechanism is easily laid bare."

Th. Ribot, 1882.

A Taxonomy of Memory

One of the most important developments in understanding the neurological basis of memory has been the recognition that memory is not a single, homogenous entity, but rather is comprised of several relatively distinct yet mutually interacting systems that differ from one another in the type of information stored and/or in the processes acting upon that information.

One fundamental distinction has been made between long-term memory and short-term or working memory. Working memory is a limited-capacity (i.e., able to hold only about seven recognizable items) system that is capable of storing and manipulating information for short periods of time (i.e., about 20 to 30 seconds) without rehearsal; with rehearsal, information can be maintained in working memory indefinitely. In contrast, long-term memory appears to be virtually unlimited in capacity, and capable of storing the experiences, factual knowledge and skills over an entire lifetime.

Working memory can be subjectively viewed as the information one is immediately thinking about or working on, and more formally viewed as the currently active subset of long-term memory. Working memory consists primarily of a central executive system (or supervisory attentional system) that is aided by two subsidiary slave buffer systems; one (the visuo-spatial scratchpad) for holding visuospatial information and the other (the phonological loop) for holding speech-based information.

Further distinctions have been made between different long-term memory systems, each with its own special functions and organization. One memory system dichotomy that has generated considerable theoretical and empirical interest is the distinction between declarative and procedural memory. Declarative memory refers to knowledge of episodes and facts that can be consciously recalled and related (i.e., declared) by the rememberer. It has been characterized as "knowing that" and includes such things as memory for the words on a recently presented list and knowledge that a cat is an animal. Procedural memory, in contrast, is described as "knowing how" and pertains to

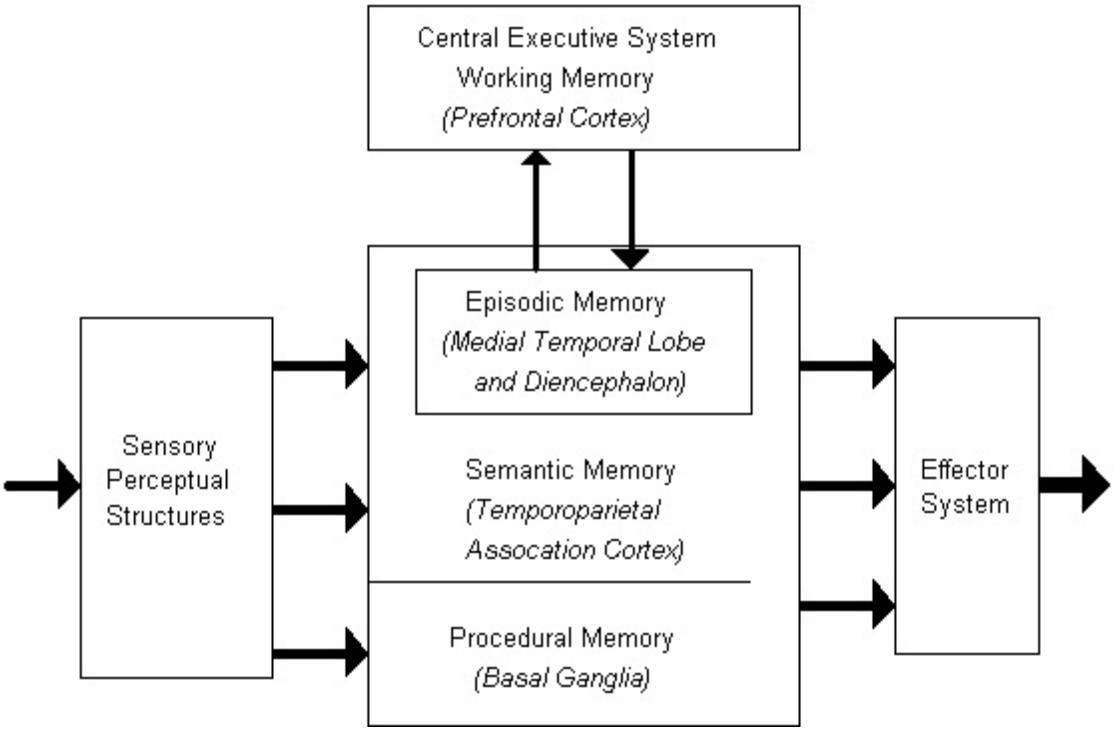
an unconscious form of remembering that is expressed only through the performance of the specific operations comprising a particular task. The use of procedural memory is indicated by the performance of a newly acquired motor, perceptual, or cognitive skills.

Declarative memory can be further divided into episodic and semantic forms. Episodic memory refers to information that is remembered within a particular temporal and/or spatial context. For example, remembering what you had for breakfast this morning or when you last saw a physician would require retrieval from episodic memory. Most of the traditional verbal learning techniques used in cognitive psychology involve retrieval from episodic memory. For instance, when you read a list of words to a subject and then ask him or her to recall the words a minute later, the patient must retrieve a specific list of words presented in a specific temporal (1 minute previously) and spatial (same examining room) context. Recall of any list of words encountered during his or her lifetime would not be appropriate or correct. (e.g., remembering a list of words presented 10 minutes ago).

Semantic memory, on the other hand, refers to one's fund of general knowledge that is not dependent upon contextual cues for its retrieval (e.g., knowing that a cat is an animal with four legs). For example, asking how many feet are in a yard, the name of the first president of the United Sates, or the capital of California would all involve retrieval from semantic memory. In each case, the specific information can be retrieved without recalling the particular episode in which that information was acquired. Semantic memory has been proposed to exist as a representation of knowledge based on an organized network of inter-related categories, concepts and attributes.

The Neuropsychology of Memory

Studies of memory in brain-damaged populations have generally validated this psychological model of memory, and have also served to identify the neuroanatomical structures associated with different memory systems.



Medial Temporal Lobe System: Consolidation of Episodic Memories

Support for the distinction between declarative and procedural memory has primarily come from patients with circumscribed amnesia arising from damage to medial temporal lobe or midline diencephalic brain structures.

The most striking feature of amnesic patients' severe memory impairment is their anterograde amnesia, or their inability to acquire new verbal and nonverbal information. This profound memory impairment occurs despite a relative preservation of all other intellectual capacities. An amnesic patient:

"...gives the impression of a person in complete possession of his faculties; he reasons about everything perfectly well, draws deductions from given premises, makes witty remarks, plays chess or a game of cards, in a word, comports himself as a mentally sound person. Only after a long conversation with the patient, [you] may note that at times he utterly confuses events and that he remembers absolutely nothing of what goes on around him; he does not remember whether he had his dinner, whether he was out of bed. On occasion the patient forgets what happened to him just an instant ago; you came in, conversed with him, and stepped out for one minute; then you come in again and the patient has absolutely no recollection that you had already been with him. [The patient] may read the same page over and over again sometimes for hours, because he is absolutely unable to remember what [he has] read. In conversation he may repeat the same thing 20 times, remaining wholly unaware that he is repeating the same thing."

Korsakoff, 1889.

Despite their severe anterograde memory deficits, however, amnesic patients

demonstrate normal working memory and procedural memory (i.e., an intact ability to acquire and retain skills), along with a preservation of premorbid semantic memory (i.e., an intact general fund of knowledge).

In addition to their anterograde amnesia, amnesic patients also display a variable degree of retrograde amnesia, or impairment of memory for events that were acquired normally prior to the onset of amnesia. Regardless of the temporal extent (i.e., months, years or decades) of their retrograde amnesia, however, most amnesic patients demonstrate a temporal gradient, with recent memories more impaired than remote memories. Although the reasons for the existence of a temporal gradient are not entirely clear, one possibility is that older memories, through repeated re-activation and rehearsal, become over learned and consequently become increasingly a part of semantic memory. More recent memories, in contrast, will remain almost entirely as episodic memory. In this view, the temporally graded retrograde amnesia can be seen as an extension of amnesic patients' impaired episodic but intact semantic memory.

Taken together, studies with amnesic patients suggest that the acquisition and retention of episodic memories are critically dependent upon the medial temporal lobe (i.e., hippocampus, amygdala, enthorhinal cortex and parahippocampal cortex) and related diencephalic (i.e., the dorsomedial nucleus of thalamus and the mammillary bodies of the hypothalamus) regions damaged in these patients.

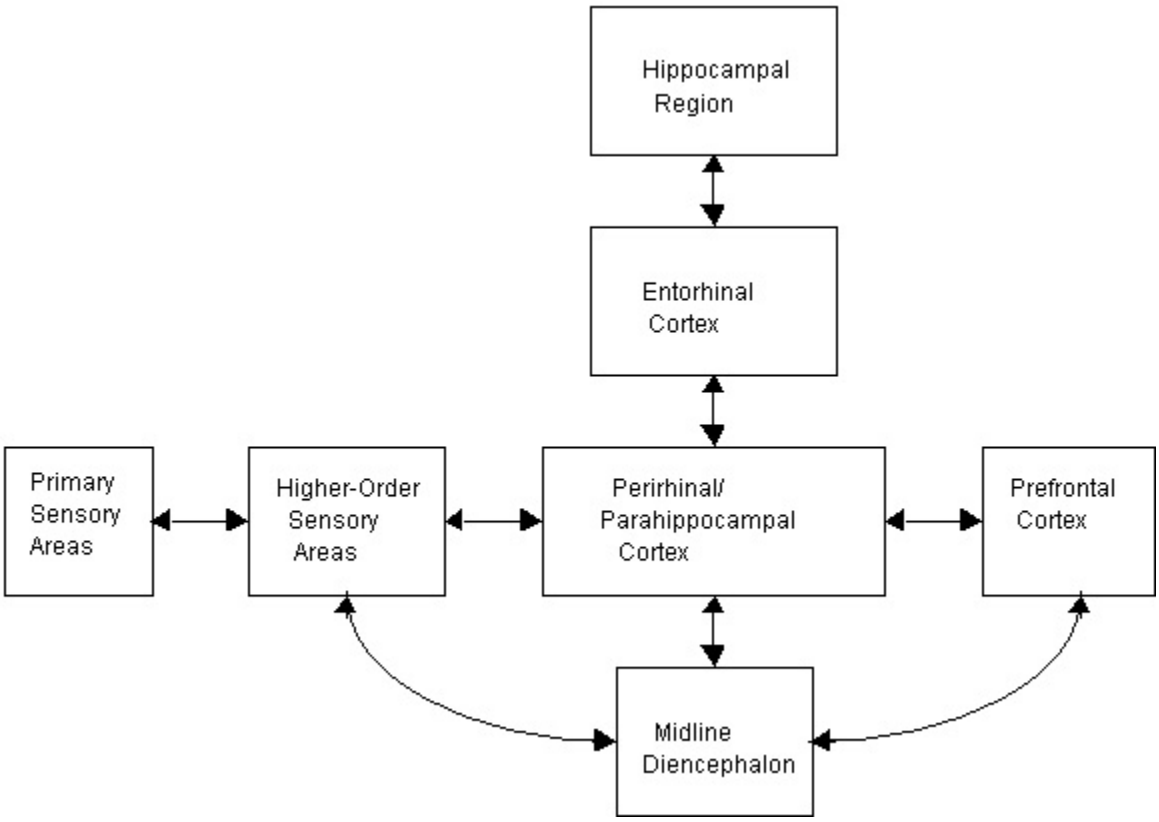
In this view, actual memory representations are established and maintained in the neocortex. The medial temporal lobe system, damaged in amnesics, directs consolidation of episodic memories within neocortex by gradually binding together the multiple, geographically separate cortical regions that together store memory for a whole event. This binding or integration is achieved through the reciprocal pathways connecting the hippocampus via the entorhinal cortex to the cortical modules.

Prefrontal Cortex: Central Executive System and Working Memory

A number of recent studies have indicated that damage to the prefrontal cortex in humans can produce impairments in memory that are distinguishable from the memory deficits that are classically observed following medial temporal lobe damage. While amnesic patients with medial temporal lobe damage are characterized by an inability to acquire and retain new information and experiences, patients with frontal lobe damage appear to be able to store new information in a normal fashion, but have difficulty manipulating both new and old memories in a strategic manner. Thus, frontal patients can perform normally on recognition memory tests for previously presented

items, yet display significant impairments in their ability to: 1) make judgments about the temporal presentation of these items; 2) make metamemory judgments about their ability to successfully identify these items on a subsequent recognition test, and 3) identify the source from which these items were acquired.

Taken together, these studies suggest that the prefrontal cortex may be part of the central executive or working memory system that is responsible for the coordination of planning, elaborative and organizational processes which facilitate encoding and retrieval of information within the medial temporal lobe system.



Neocortical Association Areas and Semantic Memory

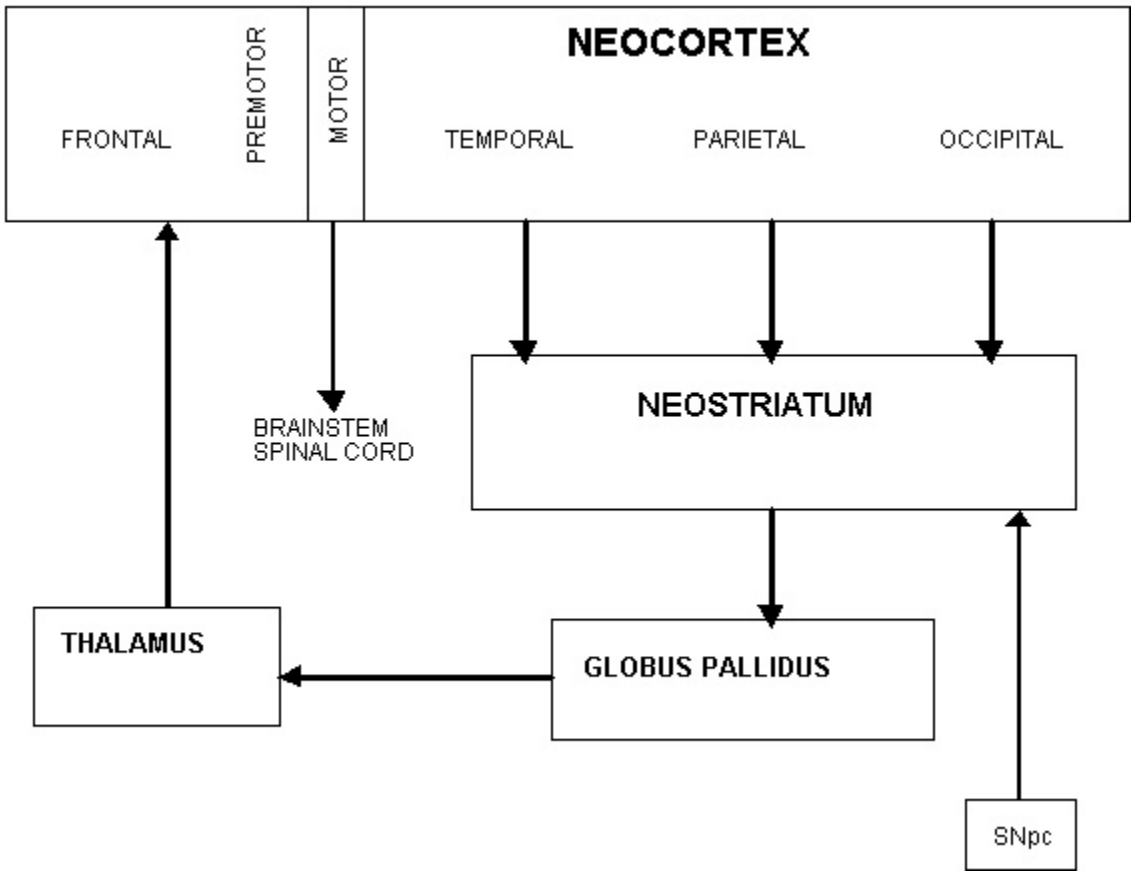
The observation that amnesic patients with severe episodic memory impairment often have normal semantic memory suggests that semantic memory is mediated by a neurobiological systems that are distinct from the medial temporal lobe system mediating episodic memory. Indeed, recent functional imaging studies as well as studies of patients with focal brain lesions indicate that semantic knowledge may be stored in a distributed fashion in neocortical association areas, particularly in the lateral temporal lobes.

A number of studies have reported patients suffering from progressive degenerative brain disease who present primarily with semantic memory impairments. These "semantic dementia" patients typically display prominent loss of semantic memory knowledge while other aspects of language (e.g., syntax, phonology), episodic memory, and other cognitive functions are relatively preserved. The neuropathological changes seen in semantic dementia are focused in the temporal lobes, often affecting the left more than the right.

In addition to generalized impairments of semantic memory, specific aspects of semantic memory (such as particular semantic categories) can also be selectively impaired. For example, patients have been observed who display selective impairments in knowledge about animate but not inanimate objects, while other patients have displayed the opposite pattern of impairment. One possible explanation for these striking dissociations is that semantic memory is not stored in discrete brain regions that are separate from the various sensorimotor modalities used in perception and action, but may in fact consist of distributed representations within the sensorimotor systems themselves. In this view, animate and inanimate objects may differ from one another in their reliance on knowledge from different sensorimotor modalities, with animate objects being known predominantly by their visual and other sensory attributes and inanimate objects being known predominantly by their function (i.e., abstract motoric representations). Thus, selective impairments in animate or inanimate objects may be attributable to selective damage of those brain regions mediating visual or motoric processes, respectively.

Basal Ganglia and Procedural Memory

The demonstration that amnesic patients can acquire and retain motor, perceptual and cognitive skills despite their severe episodic memory deficits provides strong evidence that procedural memory is not critically dependent upon the medial temporal lobe and midline diencephalic structures damaged in amnesia. Rather, a number of recent studies with patients with basal ganglia dysfunction (e.g., Huntington's disease and Parkinson's disease patients) have indicated that procedural memory is mediated, at least in part, by a corticostriatal system involving reciprocal connections between neocortex and basal ganglia. In particular, damage to the corticostriatal system has been found to produce impairments in perceptuomotor skill learning and other tasks which involve the generation and refinement (i.e., learning) of motor programs to guide behavior. Moreover, Huntington's and Parkinson's disease patients have also recently been found to be severely impaired on a probability classification learning task analogous to habit learning tasks used in animal studies. Taken together, these findings indicate that the corticostriatal system is critically involved not only in the learning of motor skills and central motor programs, but can more generally be thought of as a procedural or habit learning system even when motor skill learning is not required.



THE AMNESIC SYNDROME

Medial Temporal Lobe (e.g. Hippocampal) or Midline Diencephalic Damage

- Hypoxic Ischemia

- Vascular Accident

- Alcoholic Korsakoff's Disease

STATUS OF MEMORY SYSTEMS BEHAVIORAL PRESENTATION

Impaired Episodic Memory:Severe Anterograde Amnesia
- Consolidation Deficit
- Rapid Forgetting
-Temporally-Graded Retrograde Amnesia
-Intact Semantic Memory:Intact Fund of Knowledge
-Intact Procedural Memory:Intact Skill Learning

FRONTAL LOBE AMNESIA

STATUS OF MEMORY SYSTEMSBEHAVIORAL PRESENTATION

Impaired Central Executive System:Mild Anterograde Amnesia
- Impaired Retrieval
- Impaired Temporal Order Judgments - Impaired Source Judgments
- Impaired Metamemory Judgments

-Intact Semantic Memory:Intact Fund of Knowledge
-Intact Procedural Memory:Intact Skill Learning

ALZHEIMER'S DISEASE

Progressive Dementia

Cortical Atrophy and Neuronal Loss
- medial temporal lobe structures
- temporoparietal association cortices

Neurofibrillary Tangles and Neuritic Plaques
Cholinergic and Noradrenergic Deficits

STATUS OF MEMORY SYSTEMSBEHAVIORAL PRESENTATION

Impaired Episodic Memory:Severe Anterograde Amnesia
- Consolidation Deficit
- Rapid Forgetting

Temporally-Graded Retrograde Amnesia

Impaired Semantic Memory:Impaired Fund of Knowledge

Intact Procedural Memory:Intact Skill Learning

HUNTINGTON'S DISEASE

Involuntary Choreiform Movements
Progressive Dementia
Atrophy of Neostriatum

STATUS OF MEMORY SYSTEMSBEHAVIORAL PRESENTATION

Impaired Central Executive System:Moderate Anterograde Amnesia
- Impaired Retrieval
- Impaired Temporal Order Judgments - Impaired Source Judgments
- Impaired Metamemory Judgments

Moderate, Flat Retrograde Amnesia

Intact Semantic Memory:Intact Fund of Knowledge

Impaired Procedural Memory:Impaired Skill Learning